discussion with the examiner. For example, the claims have been amended to delete any reference to "therapy", "pathogen" or "treatment of disease", and to refer to the cells in a patient to be killed. By so doing, it was agreed that applicants did not have to demonstrate a therapeutic efficacy, only that the claimed method was effective in killing the targeted cells. The limitations of claims 4 and 25 have been incorporated into claim 1 and claims 4 and 25 cancelled. Claim 26 was also cancelled as duplicative. Claims 5 and 6 were amended to properly depend from claim 1. Claim 27 was amended to properly characterize and limit the claimed Markush group.

Rejection Under 35 U.S.C. § 112, first and second paragraphs

Claims 1-4, 14-18, 25-26, and 28-29 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention and lack of written description. Applicants respectfully traverse these rejections to the extent that they are applied to the claims as amended.

As discussed at the interview, the primary issue was the question of therapeutic efficacy, not whether or not the method is effective at killing cells. Indeed, this is amply demonstrated by the examples. The secondary issue is the breadth of the claims. As the examiner noted, this can be met by a showing that more than one species of antigen, indicative of the breadth of the genus, can be targeted using the CTLs to kill cells having the antigens on their surfaces.

As discussed at the interview, the application contains a number of specific examples of antigens. See, for example, pages 17-18. As briefly described at pages 39-41 (more details are

provided in the examples beginning at page 42), and shown by the data in Figures 1 and 2, an antigen can be an antigen such as mdm-2, presented by a virus-induced tumor cell, RMA (see page 44, lines 12 and 13). Mdm-2 is a normal cellular protein which is expressed at abnormally high levels in tumours (see page 7, line 5). The antigen can also be a viral antigen (example 2, page 52) or a tumor antigen (pages 17-18). The RMA cells were killed in mice. Figure 3 shows the data for CTL mediated killing where the CTLs are specific for an mdm 100 peptide present on tumor cells (this peptide is derived from the mdm-2 protein that is a self protein overexpressed in tumors); Figure 4 shows the data for killing of melanoma cells by CTLs targeted to the mdm100 peptide. See also Figure 6. Page 41, page 57, line 26 to page 58, line12 and Figure 7 shows the data for CTL mediated killing of cells having on their surface HLA-A0201-binding cyclin D1 peptide (101-110), which is derived from the cyclin-D1 protein that is overexpressed in tumours but also expressed in normal cells . This data is particularly striking because it shows one can kill a cell presenting what would otherwise not be an antigen (i.e., a normal protein) on the surface of the targeted cells IF the antigen is presented within the context of a mismatched HLA. In this example, CTLs with the specified characteristics were made to a selected antigen, in this case cyclin D1, which is known to be overexpressed in a variety of tumours (see page 7, line 4)]

This data shows that the method was effective to kill tumor cells but not normal cells where the CTLs were targeted to normal proteins that were overexpressed in tumor cells.

Accordingly, it is believed that applicants have demonstrated the general applicability of the claimed method.

Since the application was filed, the inventor has made CTLs using the protocol described in the application against proteins such as WT1, CD45 and CD68 that are present at higher levels in tumours but also found in normal cells]

The claims have been amended as discussed at the interview to use language the examiner thought was clear and supported. The undersigned would greatly appreciate a call to work out any further required changes in language to place the case in condition for allowance.

Allowance of claims 1-3, 5-18, and 27 is respectfully solicited.

Respectfully submitted,

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